CDC Responses to recommendations made in the Institute of Medicine report, *Vaccine Safety Research, Data Access, and Public Trust* (February 2005)

In 2004, the Centers for Disease Control and Prevention (CDC) asked the Institute of Medicine (IOM) to establish a Committee on Review of the National Immunization Program's Research Procedures and Data Sharing Program. The Committee was charged with providing 1) a review of the Vaccine Safety Datalink Data Sharing Program and recommendations to facilitate use, ensure appropriate utilization and protect confidentiality, and 2) a review of the iterative approaches to conducting analyses used by the Vaccine Safety Datalink (VSD) Research Project, a review of the procedures for the release of preliminary study findings from the VSD Research Project, and recommendations on the release of preliminary findings in the future.

In February 2005, the IOM released its review and recommendations in the report *Vaccine Safety Research, Data Access, and Public Trust*. This document restates below each of the recommendations made by the IOM Committee and provides CDC's responses to each recommendation.

Since undertaking this review of CDC's vaccine safety research and data sharing program procedures, CDC has taken steps to further strengthen its vaccine safety activities. These steps have included organizational changes which affect the response to the recommendations made in this report.

In March 2004, the administration of the VSD Data Sharing Program was transferred from CDC's National Immunization Program (NIP) to CDC's National Center for Health Statistics (NCHS). The NCHS has extensive experience in providing researchers with access to NCHS databases through its Research Data Center (RDC). Following the transfer of the administration of the Data Sharing Program, CDC collaborated with the VSD-participating managed care organizations (MCOs) to revise the NCHS RDC Data Sharing Guidelines. The NCHS RDC Data Sharing Guidelines currently include provisions to access the VSD data which are consistent with the established policy for accessing the various datasets available at the NCHS RDC. The requirements for access to VSD data are listed as an appendix in the NCHS RDC Data Sharing Guidelines. Some of the recommendations made by the IOM Committee regarding the Data Sharing Program are now applicable to NCHS and its RDC.

The CDC Executive Leadership Board has taken additional steps to further enhance the nation's immunization safety efforts by relocating the immunization safety activities, including the Vaccine Safety Datalink activity, from CDC's NIP to CDC's Office of the Chief Science Officer (OCSO). CDC took these steps to build a more robust immunization safety activity to keep pace with the increasing number and combinations of recommended immunizations, especially for children under two. In early April 2005, CDC notified Congress of this decision, and on April 21, the relocation of the immunization safety activities to OCSO became official. The new name of the office is the Immunization Safety Office (ISO). Collaboration between the Office of the Chief Science Officer's ISO and other CDC components (such as the NIP, the National Center for Infectious Diseases, etc.) on immunization safety issues is essential to protect the public health and will continue. Many of the IOM recommendations that refer to NIP are now more applicable to ISO/OSCO.

CHAPTER 2: DESCRIPTION OF THE VACCINE SAFETY DATALINK

The Committee reviewed the purpose of and mechanism for funding the Vaccine Safety Datalink research project. Based on its review, the Committee made the following recommendation:

Recommendation 2.1: The committee recommends that the NIP and NCHS seek legal advice to clarify the applicability of the Shelby Amendment and the Information Quality Act to VSD data and VSD preliminary findings.

This recommendation has been implemented.

The Shelby Amendment is inapplicable to this contract data. Regarding the Information Quality Act, CDC carefully complies with its Information Quality Guidelines, which are available on the HHS website at http://aspe.hhs.gov/infoquality/Guidelines/cdcinfo2.shtml, to ensure the quality of the information it is disseminating.

CHAPTER 3: THE VACCINE SAFETY DATALINK DATA SHARING PROGRAM

The Committee reviewed the guidelines for public access to the Data Sharing Program at NCHS that provides access to VSD data. As described above, in March 2004 the administration of this Data Sharing Program was transferred from NIP to NCHS. The charge to the Committee was revised following the transfer of the administration of the Data Sharing Program at NCHS that provides access to VSD data to include NCHS in its review and recommendations.

Following its review of the Data Sharing Program at NCHS that provides access to VSD data, the Committee made the following recommendations:

Recommendation 3.1: The committee recommends that future revisions of the VSD data sharing guidelines clearly and explicitly describe the VSD data that are and are not available to independent external researchers for new vaccine studies through the VSD data sharing program.

This recommendation has been implemented.

Appendix IV of the NCHS RDC Data Sharing Guidelines has been revised to clearly state that the VSD data available through the Data Sharing Program are final datasets from published studies and VSD data through December 2000 for new vaccine safety studies. These data were purchased under a contract with the MCOs and therefore are accessible to CDC and external researchers who follow RDC procedures. Data from the VSD Research Project collected after December 2000 are not available through the Data Sharing Program. To enhance the privacy protections of their enrollees and the proprietary concerns of the MCOs, the MCOs took control of access to the VSD database after December 2000. These data can be accessed through a formal collaboration with an MCO. The external researcher must work through MCO procedures. Any such collaboration is at the discretion of the MCOs. CDC cannot guarantee external investigators' ability to gain access to the VSD data held by the MCOs.

To understand why access to pre and post 2000 data is different, it is important to provide some additional background. Many of the participating MCOs had serious concerns regarding the potential release of raw data to individuals outside of the VSD Project. If the MCOs were not provided assurances regarding the protection and confidentiality of their patient level data, many,

if not all of the participating MCOs would reconsider their involvement in the VSD Project. The impact of losing the VSD Project as a national and international source for monitoring vaccine safety in a scientifically rigorous manner cannot be overstated. It is considered to be the largest database available in the world for objectively assessing vaccine safety issues. It needs to be recognized that a larger societal good is served when individuals and organizations feel confident in reporting information without compromising the privacy of the information that they provide.

Recommendations 3.2: The committee recommends that the distinction between the annual automated VSD data (whose quality cannot always be guaranteed) available to independent external researchers through the data sharing program and the study-specific data potentially available to researchers affiliated with the NIP or the participating MCOs be explained more clearly in the data sharing guidelines so that potential users are informed about the limitations of the data that are available through the data sharing program.

This recommendation has been implemented.

Appendix IV of the NCHS RDC Data Sharing Guidelines has been revised to clearly state that the data collected for the VSD Research Project (that can be accessed through the RDC) have been created from MCO administrative data which were not collected primarily nor soley for the purpose of scientific research. These data were primarily collected for clinical care and administrative purposes. Because such data were not collected using research data collection methodologies, the Guidelines note that the quality of the data cannot be guaranteed. Potential data discrepancies and varying degrees of data quality that are inherent to databases like the VSD do exist and are not resolvable with data that are available in the RDC.

Recommendation 3.3: Because of the limitations in the data available to independent external researchers through the VSD data sharing program, the committee recommends that the NIP require the designation of a facilitator for collaboration at each MCO as a condition of the VSD contract.

This recommendation cannot be implemented for the following reasons:

- NCHS serves as the primary contact/ facilitator for external researchers within the Data Sharing Program
- The MCOs do not currently have the capacity or funding to provide a facilitator for the purposes of the Data Sharing Program
- Imposing additional requirements on the MCOs that participate in the VSD Research Project is a disincentive to participate in the VSD Research Project and threatens the continued viability of this project which has proven to be an important resource for vaccine safety data for the nation. See 3.1 above regarding the fragility of the VSD Project. If the MCOs were not provided assurances regarding the protection and confidentiality of their patient level data, many, if not all of the participating MCOs would reconsider their involvement in the VSD Project. The impact of losing the VSD Project as a national and international source for monitoring vaccine safety in a scientifically rigorous manner cannot be overstated. It is considered to be the largest database available in the world for objectively assessing vaccine safety issues.

The Data Sharing Program at NCHS that provides access to VSD data is independent from the research activities conducted through the VSD Research Project (i.e., the VSD Research Project is supported through a contract with America's Health Insurance Plans).

Direct collaboration between external researchers and VSD researchers is already possible at the sole discretion of the MCOs.

Recommendation 3.4: To formulate alternative hypotheses or to conduct alternative analyses, researchers need to have access to information or variables that would allow the use of different inclusion and exclusion criteria, different variables for inclusion in models, and, in general, earlier versions of a dataset that would support such restructuring. The committee believes that it is appropriate to allow independent external researchers access to such datasets and recommends that such datasets be made available through the VSD data sharing program.

This recommendation will be implemented.

It is currently possible for researchers to have this type of access for VSD data collected through 2000 that are residing at the RDC. In regard to published VSD studies, currently only final datasets are available for reanalysis. Datasets for future studies conducted by VSD researchers will be created to allow external researchers flexibility in conducting reanalyses to the extent possible and practical.

All final datasets and documentation for studies published after August 2002, are archived at the MCOs. Beginning in June 2005, VSD data from VSD research project abstracts accepted and presented at scientific meetings, as well as public meetings have been archived and will be made available after publication through the Data Sharing Program at NCHS upon request.

Recommendation 3.5: The committee recommends that the VSD data sharing guidelines reflect a more specific categorization of the types of studies that can be done with VSD data to conceptualize the full range of studies that independent external researchers may wish to conduct with the data: an audit, a broader reanalysis, a corroboration study, and an investigation of a new hypothesis.

This recommendation has been implemented.

Appendix IV of the NCHS RDC Data Sharing Guidelines has been revised to clearly state that external researchers may conduct a reanalysis of a published VSD study or a new investigation of a vaccine safety hypothesis with data that are resident at the RDC. For external researchers wanting to access data from January 2001 and beyond for a new vaccine safety study, they will need to establish a formal collaboration with a MCO and work in accordance with MCO procedures. Collaboration is at the sole discretion of the MCOs. Such collaboration would be outside the scope of the VSD Data Sharing Program and, therefore, data would not be accessed at the RDC.

Recommendation 3.6: The committee recommends that there be specific evaluation criteria for VSD proposals and that interested persons have an opportunity to comment on the draft evaluation criteria before they are finalized; the evaluation criteria should be identified clearly in the VSD data sharing guidelines.

This recommendation has been implemented.

Appendix IV of the NCHS RDC Data Sharing Guidelines has been revised to include specific evaluation criteria for VSD proposals as recommended in the IOM data sharing report. Additionally, the NCHS RDC Data Sharing Guidelines were published in the Federal Register for an extended period of time to allow for public comment.

The NCHS RDC Data Sharing Guidelines evaluation criteria for VSD proposals include the following:

- Scientific and technical feasibility of the project
- Availability of resources at the RDC
- Risk of disclosure of restricted information

Recommendation 3.7: The committee recommends that the technical feasibility of a proposed VSD study be the primary evaluation criterion in the review of proposals submitted to the VSD data sharing program.

This recommendation has been implemented.

Appendix IV of the NCHS RDC Data Sharing Guidelines has been revised to indicate that technical feasibility is the primary evaluation criterion for the review of proposals submitted to the VSD Data Sharing Program. All proposals are reviewed to determine if the requested data are available within the VSD data base.

Recommendation 3.8: To assist independent external researchers who want to use VSD data through the data sharing program, the committee recommends that the NIP and NCHS add to the VSD data sharing program guidelines a list of recommended competencies for VSD data analysis.

This recommendation has been implemented.

The NCHS RDC Data Sharing Guidelines have been revised to state that researchers are expected to have competencies in areas such as the ability to analyze health outcomes data, the ability to analyze large databases, and the ability to use one or more statistical packages.

Recommendation 3.9: To facilitate use of the VSD data sharing program, the committee recommends that the NIP work with the VSD-participating MCOs to determine the feasibility of using IRB authorization agreements for VSD research proposals.

Activities are underway to explore the feasibility for the implementation of this recommendation.

Discussions are underway with each of the MCO IRBs to explore the possibility and feasibility of creating a more streamlined process for IRB review.

Recommendation 3.10: The committee recommends that the NIP work with the MCOs participating in the VSD and America's Health Insurance Plans (the VSD contractor) to evaluate the feasibility of streamlining the IRB review process for audits or broader reanalyses in accordance with appropriate regulations.

Activities are underway to explore the feasibility for the implementation of this recommendation. Specifically, discussions are occurring with each of the MCO IRBs to explore the possibility and feasibility of creating a more streamlined process for IRB review.

Recommendation 3.11: Because the confidentiality concerns are integral to the continuation of the VSD, the committee recommends that NCHS in conjunction with the MCOs develop policies and procedures to address confidentiality violations of VSD data and that they be clearly described in the VSD data sharing program guidelines and the agreements that external researchers must sign before using the RDC.

This recommendation has been implemented.

The protection of confidential data is addressed strongly in the NCHS RDC Data Sharing Guidelines. In particular, the confidentiality agreement documents (Appendices V and VI) of the NCHS RDC Data Sharing Guidelines include provisions to address the issue of confidentiality violations.

Recommendation 3.12: The committee concludes that it is reasonable to expect researchers who request access to VSD data have their own funding and it therefore recommends that RDC costs not be waived for independent external researchers.

This recommendation has been implemented.

The NCHS RDC Data Sharing Guidelines include a section on costs for use of the RDC.

Recommendation 3.13: The committee recommends that, as a condition of accessing VSD data, independent external researchers that use the VSD data sharing program be required to submit a report to the NIP (with a copy to NCHS) within a reasonable time (to be determined by the NIP) on the status of their study, the type of study conducted (an audit, a broader reanalysis, a corroboration study, or an investigation of a new hypothesis), the results obtained, and their planned further activities. The reports should be made public by the NIP and should be easily accessible.

This recommendation cannot be implemented for the following reasons:

- NCHS does not require progress reports from any external researchers accessing data at the Research Data Center (RDC) and therefore would not require progress reports for those researchers accessing only VSD data
- In general, requiring progress reports from external researchers on status of their study, type of conducted, results obtained, etc. would be considered intrusive to external researchers
- Requiring progress reports could add additional costs to external researchers in accessing data at the RDC because NCHS staff would have to monitor, track and process such reports.
- Although NCHS does not require status reports from independent external researchers accessing RDC data, researchers that would like to provide status reports on studies involving VSD data can do so. Such reports should be submitted to NCHS and could address the type of study conducted, the results obtained, and planned further activities. Appendix IV of the NCHS RDC Data Sharing Guidelines has been revised to clarify that researchers may provide status reports on studies involving VSD data.

Recommendation 3.14: The committee recommends that, as a condition of accessing VSD data, all independent external researchers that use the VSD data sharing program be required to submit to the NIP (with a copy to NCHS) a copy of a manuscript intended for publication at least 30 days before submission to a journal or other print or electronic media. Copies of presentations to be delivered at conferences or meetings that are open to the public or that have media coverage should also be submitted to the NIP and NCHS at least 15 days before presentation.

This recommendation has been implemented in part.

Appendix IV of the NCHS RDC Data Sharing Guidelines has been revised to clearly state that a copy of the manuscript must be received by NCHS 30 days before submission to a journal or other print or electronic media. NCHS does not currently require submission of presentations and therefore does not plan to change this section of the NCHS RDC Data Sharing Guidelines as it would be inconsistent with general NCHS policies.

CHAPTER 4: THE VACCINE SAFETY DATALINK RESEARCH PROCESS AND THE RELEASE OF PRELIMINARY FINDINGS

The Committee reviewed the iterative approaches to conducting analyses that are characteristic of studies using the complex, automated VSD system. The Committee reviewed the VSD research processes and its processes for the release of preliminary findings from VSD studies. Based on its review, the Committee made the following recommendations:

Recommendation 4.1: To enhance the value of the VSD, to improve the credibility of results derived from it, and to support the Centers for Disease Control and Prevention's role in assessing vaccine safety, the committee recommends that the NIP develop an annual VSD research plan. The plan should define the priorities for new studies and support of current studies. The annual VSD research plan should be made public. Material deviations from the plan should be identified and be publicly available.

This recommendation has been implemented.

Priority studies and current vaccine safety studies will be highlighted on the CDC website. Study status and proposed timeline for completion will be included for each priority study. Ultimately, CDC would hope to develop and publish a broader vaccine safety plan, not just a VSD Research Plan.

Recommendation 4.2: To support greater use of the VSD and to promote opportunities for collaborative work outside the existing community of VSD researchers, the committee recommends that the annual VSD research plan include provisions for allocating some existing funds, on a competitive basis, to external researchers interested in conducting collaborative work with VSD data.

This recommendation cannot be implemented at this time.

The feasibility of implementing such a program would require consideration of the following:

- The availability of resources to fund external researchers
- The establishment and funding of a process for the peer review of proposals and the determination of awards
- The procedures and support for assisting external researchers who are not awarded CDC funds, yet still want access to VSD data
- The policies and procedures for addressing external researchers who are awarded funds, but are not willing to collaborate with MCO investigators

However, CDC is willing to discuss with AHIP and MCOs the potential costs of implementing such a program as well as the MCOs' willingness to enter into collaborative projects with external researchers. CDC is also willing to explore with HHS and its appropriators the possibility of creating an extramural grant program.

Recommendation 4.3: The committee recommends that detailed research protocols for each study conducted by an internal VSD researcher be developed, peer-reviewed, and archived. Each protocol should include well-specified definitions of the study population, exposures, and cases; detailed analytic plans; sample size requirements; and study timelines. Data collection forms, procedures, data and analysis files, programming code, and database versions should be documented, cataloged, and archived for a period of at least 7 years after completion of a study.

This recommendation has been implemented.

As part of standard scientific practice, VSD researchers create well-defined proposals for their studies. When studies are complete, the VSD Research Project requires that these detailed proposals be archived. The archived material includes study documentation, data collection forms, IRB approvals, computer programs, and study datasets. These materials are located at the lead MCO site and can be made available to NCHS upon request.

Recommendation 4.4: To promote collaboration and information-sharing, the committee recommends that the NIP update and improve its list of publications and presentations by establishing a VSD research clearinghouse that provides on a timely basis status reports, study findings, and conclusions for current and completed VSD studies.

This recommendation has been implemented.

An updated VSD Research Project publication list will be posted to the CDC website. VSD will also highlight priority studies on the CDC website.

The feasibility of establishing a research "clearinghouse" will require further discussion within CDC as well as with the MCOs. In the interim, VSD will update the status of priority studies posted on the CDC website on a regular basis.

Recommendation 4.5: The committee recommends that the NIP and NCHS release publicly the procedures that will be used for record-keeping of VSD data sharing program documents and update the status of the program regularly.

This recommendation can be partially implemented. The record-keeping procedures relative to the RDC are generally consistent with the approach used for public use files since the RDC was created as an alternative mode of providing access when public use files were not sufficient. Records are maintained for internal purposes (such as to assure that we can adequately provide service), are not used to monitor overall use of data sets, and are not structured in a way that would be useful to the public. However, NCHS is in the process of improving the tracking system for RDC projects that would allow for the tracking of projects by data set. Although this information is still for internal use, the RDC could respond to specific requests for information on the number of projects that use the VSD if necessary.

Recommendation 4.6: The committee recommends that in nearly all situations preliminary findings from the VSD be subject to independent external peer review before being communicated to the public or used as the basis of a policy decision. When CDC determines that purely internal peer review is necessary before release, external peer review should be undertaken as soon as possible.

While CDC appreciates the utility of external peer review and utilizes it extensively, this recommendation cannot be fully implemented.

Discussions may need to take place at all levels of HHS and with its Operating Divisions to address policies and procedures regarding release and use of preliminary findings from any particular study. Policies and procedures may vary depending on the situation, e.g., a release for

a public health emergency response may require a different process than a release for a scientific meeting. In addition, in some cases, the process described in the new OMB Quality Bulletin for Peer Review may need to be followed.

Recommendation 4.7: The committee recommends that preliminary findings from VSD data be shared with the public whenever the findings are presented to anyone *other than* collaborators in the research, federal employees responsible for research activities, MCO-affiliated VSD researchers, scientific journals, peer reviewers for scientific journals, and people responsible for oversight of the research.

This recommendation is too restrictive and cannot be implemented.

Discussions may need to take place at all levels of HHS and with its Operating Divisions to address policies and procedures regarding release and use of preliminary findings from any particular study. Policies and procedures may vary depending on the situation, e.g., a release for a public health emergency response may require a different process than a release for a scientific meeting. In addition, in some cases, the process described in the new OMB Quality Bulletin for Peer Review may need to be followed.

Recommendation 4.8: The committee recommends that preliminary findings from VSD data be shared with the public whenever these findings contribute to the basis of a policy decision or are used to change guidelines on vaccine administration.

CDC appreciates the need to be as transparent as possible; however, this recommendation is so broad and restrictive that it cannot be implemented.

Discussions may need to take place at all levels of HHS and with its Operating Divisions to address policies and procedures regarding release and use of preliminary findings from any particular study. Policies and procedures may vary depending on the situation, e.g., a policy or guideline issued during a public health emergency response may require a different process than one issued by the Advisory Committee on Immunization Practices. In addition, CDC needs flexibility in determining how much data to share relative to the contribution of those data to the policy or guideline.

Recommendation 4.9: The committee recommends that when final results from VSD analyses or studies are released through publication or through presentation at a meeting, preliminary findings be shared only rarely, but that the dataset from which the final results were obtained be available to other researchers who may verify and extend the results through an audit or broader reanalysis.

This recommendation will be implemented.

The VSD Research Project has revised its internal archival guidelines to include those datasets used in the presentation of abstracts for public meetings and conferences. This policy applies to studies presented beginning August 2005 and will not apply to past VSD presentations. Such

datasets will be made available after publication of the study. External researchers will follow the same rules and regulations as outlined in the Data Sharing Guidelines.

Recommendation 4.10: The committee recommends that any preliminary findings based on VSD data that are shared with the public be put into appropriate statistical and scientific context with clear characterization of the uncertainties in the findings, of the strengths and limitations of the data, and of the possibility that new data or new analyses could change interpretations.

This recommendation will be implemented.

CHAPTER 5: INDEPENDENT REVIEW OF VACCINE SAFETY DATALINK ACTIVITIES

The Committee considered the concerns of some members of the public regarding the independence and fairness of the review of proposals submitted to the Data Sharing Program at NCHS that provides access to VSD data and the transparency of decisions made about the release of preliminary VSD study findings. The Committee found that the lack of transparency of some of the VSD processes affects the trust relationship between the National Immunization Program and some members of the public. Based on its review, the Committee made the following recommendations.

Recommendation 5.1: The committee recommends that a subcommittee of NVAC that includes representatives of a wide variety of stakeholders (such as advocacy groups, vaccine manufacturers, FDA, and CDC) review and provide advice to the NIP on the VSD research plan annually. The subcommittee charged with this role could be the existing Subcommittee on Safety and Communications or a subcommittee created specifically for the purpose.

There is currently an NVAC Vaccine Safety Subcommittee. The mission statement of this subcommittee is to consider policy options and inform NVAC discussions and recommendations regarding vaccine safety issues. In addition, the subcommittee will review the priorities of the National Vaccine Safety Plan relating to the safety of vaccines and immunizations, monitor related departmental vaccine safety priorities, and report regularly to NVAC and the department on progress of such priorities.

To ensure that there could be broad stakeholder participation in a review of the VSD research plan, CDC could be invited to present its proposed immunization safety research for the following year to the NVAC Subcommittee on Safety, supplemented by a group of technical safety experts (the expertise, number and the method of choosing these people is yet to be decided) and other interested stakeholders. It is proposed that the review be publicly announced in the Federal Register (as required) and be open to the public and that participation of public attendees in the discussion be encouraged. The review would be in the format of a "forum" or "town hall" meeting.

The subcommittee would present the outcome of the meeting to NVAC for consideration and deliberation with the potential to offer further additions or modifications for the Department to

consider. Under the NVAC Charter, the NVAC makes recommendations, and provides advice, to the Assistant Secretary for Health (ASH). The ASH would have the option of endorsing, or commenting upon, the NVAC's recommendations and forwarding them to CDC. This approach provides CDC a broad, external review process, offers the opportunity to modify the process in subsequent years, fosters full public participation, and creates maximal transparency for the process of guiding planning. If this mechanism proves useful, subsequent reviews could expand to other parts of the entire safety portfolio at CDC and/or across the Department.

Recommendation 5.2: The committee recommends that the NIP propose to the National Vaccine Program that additional liaison representatives be appointed to ensure that all perspectives are heard by adequately representing advocacy groups and other members of the public at subcommittee meetings addressing the VSD research plan.

The NVAC charter stipulates that the committee shall consist of 15 members, including the chair. Members and the chair shall be appointed by the Director of NVPO, in consultation with the National Academy of Sciences, from individuals who are engaged in vaccine safety research or the manufacturer of vaccines, or who are physicians, members of parent organizations concerned with immunizations, or representatives of states or local health agencies or public health organizations. Some members may serve in a representative status. Additionally, the recently revised charter provided for broader subcommittee membership to include individuals that may not be NVAC members:

> *"In carrying out its function, the Committee may establish subcommittees composed of members of the parent committee, as well as individuals from organizations and the public at large who are concerned and knowledgeable about immunizations and other topics pertaining to the NVAC mission."*

Recommendation 5.3: The committee recommends that an independent review committee with minimal and balanced biases and conflicts of interest be created to

- **Review independent external researchers' proposals to use VSD data through the data sharing program.**
- **Review research proposals from internal researchers and provide oversight of changes in or deviations from research protocols for internal VSD studies.**
- **Provide advice on when and how preliminary findings based on VSD data should be made public.**

This recommendation cannot be implemented at this time because the authorities and resources are not currently available. However, for two high visibility VSD research studies, panels of external independent experts already have convened to advise on and review the research protocol and monitor study progress. This process worked well and proved useful. However, this approach is labor and resource-intensive, and if implemented more broadly, would require additional resources. There may be as many as 50 studies underway at any given time with the VSD research portfolio. The recommendation also raises the question of why other vaccine safety studies outside the VSD portfolio would not benefit from external peer review. In addition, because vaccine safety studies both within and outside the VSD portfolio may involve a

range of topics requiring diverse perspectives, it is not clear that reviews by a standing committee would be preferable to *ad hoc* external peer reviews utilizing individuals with the appropriate knowledge and skills. At this time, it is only feasible to implement an *ad hoc* external peer review process for selected high impact or highly influential studies